(19) World Intellectual Property Organization International Bureau



(43) International Publication Date 17 June 2004 (17.06.2004)

PCT

(10) International Publication Number WO 2004/050635 A3

- (51) International Patent Classification⁷: A61K 31/415, 31/4164, C07D 233/56, 233/64, A61P 3/06, 3/10
- (21) International Application Number:

PCT/FI2003/000933

- (22) International Filing Date: 5 December 2003 (05.12.2003)
- (25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data: 20022159

5 December 2002 (05.12.2002) FI

- (71) Applicant (for all designated States except US): ORION CORPORATION [FI/FI]; Orionintie 1, FIN-02200 Espoo (FI).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): JÄRVINEN, Tomi [FI/FI]; Sompatie 3 I 6, FIN-70200 Kuopio (FI). NIEMI, Riku [FI/FI]; Snellmaninkatu 32 B 11, FIN-70100 Kuopio (FI). HUUSKONEN, Juhani [FI/FI]; Hillakuja 7, FIN-40340 Jyväskylä (FI).
- (74) Agent: ORION CORPORATION; Orion Pharma, Legal Affairs and Intellectual, Property Rights, P.O. Box 65, FIN-02101 Espoo (FI).

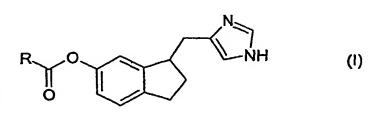
- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (regional): ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments
- (88) Date of publication of the international search report: 2 September 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: IMIDAZOL DERIVATIVES HAVING AFFINITY FOR ALPHA 2 RECEPTORS ACTIVITY



(57) Abstract: The present invention relates to novel prodrugs of MPV-2426, to methods for preparing said prodrug forms, to pharmaceutical compositions containing such prodrug forms, and to methods for using the prodrug forms. A compound of general formula (I), or pharmaceutically acceptable salts or hydrates thereof, wherein R represents unsubstituted or substituted lower alkyl, unsubstituted or substituted aryl, unsubstituted or substituted or substituted or

substituted heteroaryl, unsubstituted or substituted lower alkylamino or asaturated five or six membered heterocyclic group containing Olle or two nitrogen atoms.

International Application No PCT/FI 03/00933

A CLASSIFICATION OF SUBJECT MATTER IPC 7 A61K31/415 A61K31/4164 C07D233/56 C07D233/64 A61P3/06 A61P3/10

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

 $\begin{array}{ll} \mbox{Minimum documentation searched} & \mbox{(classification system followed by classification symbols)} \\ \mbox{IPC 7} & \mbox{A61K} & \mbox{C07D} \end{array}$

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, MEDLINE, EMBASE

		Relevant to claim No.
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Nelevant to Claim No.
Α	US 6 388 090 B1 (HUHTALA PAAVO ET AL) 14 May 2002 (2002-05-14) formula I	1-12
A	WO 97 12874 A (SAVOLA JUHA MATTI ;WURSTER SIEGFRIED (FI); HUHTALA PAAVO (FI); SAV) 10 April 1997 (1997-04-10) formula I	1-12
A	WO 01 051472 A (ORION CORPORATION) 19 July 2001 (2001-07-19) formula I	1-12
A	WO 01 30347 A (LEINO TIINA ;HEINO RIITTA (FI); ORION CORP (FI); LEHTIMAEKI TARJA) 3 May 2001 (2001-05-03) claims 1-14	1-12

X Further documents are listed in the continuation of box C.	Patent family members are listed in annex.
"A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed	"T" later document published after the International filling date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combined with one or more other such documents, such combination being obvious to a person skilled in the art. "&" document member of the same patent family
Date of the actual completion of the international search 14 June 2004	Date of mailing of the international search report 2 4 06. 2004
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentiaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer FERNANDO FARIETA / ELY

International Application No
PCT/FI 03/00933

		PC1/F1 03/00933
C.(Continua	ntion) DOCUMENTS CONSIDERED TO BE RELEVANT	
Category °	Citation of document, with Indication, where appropriate, of the relevant passages	Relevant to claim No.
P,A	WO 03 099795 A (ALLERGAN INC) 4 December 2003 (2003-12-04) example U, compound 63	1-12
A	EP 0 717 037 A (UCB SA) 19 June 1996 (1996-06-19) claim 1	1-12
		·

International application No. PCT/FI 03/00933

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This international Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. X Claims Nos.: 11-12 because they relate to subject matter not required to be searched by this Authority, namely: see FURTHER INFORMATION sheet PCT/ISA/210
2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful international Search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This International Searching Authority found multiple inventions in this International application, as follows:
As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this international Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remark on Protest The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Claims Nos.: 11-12

Claims 11-12 relate to methods of treatment of the human or animal body by surgery or by therapy/diagnostic methods practised on the human or animal body/Rule 39.1.(iv). Nevertheless, a search has been executed for these claims. The search has been based on the alleged effects of the compounds/compositions.

Information on patent family members

International Application No PCT/FI 03/00933

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
US 6388090	B1	27-12-2001	US	2001056109 A	27-12-2001
WO 9712874	Α	10-04-1997	AT	234819 T	15-04-2003
			ΑU	708002 B	2 29-07-1999
			AU	7132796 A	28-04-1997
			BG	63916 B	1 30-06-2003
			BG	102324 A	29-01-1999
			CA	2231535 A	10-04-1997
			CN		,B 11-11-1998
			CZ	9801018 A	
			DE	69626862 D	1 24-04-2003
			DE	69626862 T	2 24-12-2003
			DK	888309 T	3 22-04-2003
			EE	9800101 A	15-10-1998
			EP	0888309 A	1 07-01-1999
			ES	2195013 T	
			WO	9712874 A	
			HK	1014951 A	
			HÜ	9802927 A	
			JP	2000507914 T	27-06-2000
			ĹŤ		,B 25-09-1998
			ĹΫ	12108 A	•
			ĹΫ	12108 B	
			ЙŎ	981496 A	
			NZ	319169 A	
			PL	328167 A	
			PT	888309 T	
			RÜ		2 27-08-2002
			ŠĪ		,B 31-10-1998
			SK	43998 A	
			US	6313311 B	
			US	2002007074 A	
WO 01051472	Α	19-07-2001	AU	769896 B	
			ΑU	2853201 A	
			BR	0107644 A	
			CA	2397283 A	
			CN	1395567	
			ĒΕ	200200389 A	
			EP	1261588 A	
			WO	0151472 /	
			HU	0301008 /	
			JP	2003519688	
			NO	20023298	
			NZ	519919 /	
			SK	9982002 /	N3 04-03-2003
WO 0130347	Α	03-05-2001	ΑU	1149201	
			CA	2388979	
			ΕP	1223931	
			WO	0130347	
			JP	2003527333	
			NO	20021920	14-06-200
WO 03099795	Α	04-12-2003	MO	03099795	A1 04-12-200
		10 06 1006	AU	693614	B2 02-07-199
EP 0717037	Α	19-06-1996	AU	4036895	

Information on patent family members

International Application No PCT/FI 03/00933

Patent document cited in search report	Publication date		Patent family member(s)	Publication date
EP 0717037 A	date	BG BR CN CZ EEP FI HU JP NOZ PL SG SK US ZA	63043 B1 100208 A 9505815 A 2165133 A1 1133837 A ,B 9503271 A3 9500064 A 0717037 A1 955927 A 73980 A2 116325 A 8208622 A 955034 A 280646 A 311736 A1 113346 B1 2156239 C2 33624 A1 155095 A3 5658938 A 9510554 A	28-02-2001 31-07-1996 06-01-1998 15-06-1996 23-10-1996 17-07-1996 17-06-1996 19-06-1996 28-10-1996 28-10-1999 13-08-1996 27-08-1996 27-08-1996 24-06-1996 30-06-1998 20-09-2000 18-10-1996 05-02-1997 19-08-1997
				~